SUMMARY OF PHS ADVISORY COMMITTEE MEETING

Committee Update

Stephen D. Nightingale, M.D., Executive Secretary
Advisory Committee on Blood Safety and Availability, OASH, PHS, HHS

64th Meeting
September 16, 1999
Bethesda Ramada Inn
8400 Wisconsin Avenue
Bethesda, MD

Assistant Secretary for Health
Office of Public Health and Science
Washington D.C. 20201

DATE: September 3, 1999

TO: Interested Parties

FROM: Stephen D. Nightingale, M. D., Executive Secretary
Advisory Committee on Blood Safety and Availability

SUBJECT: Summary of August 26 and 27, 1999 Meeting

The Advisory Committee on Blood Safety and Availability met for the ninth time on August 26 and 27, 1999 at the Hyatt Regency Capitol Hill Hotel, 400 New Jersey Ave., N. W., Washington, D. C. 20001. Voting members present were Dr. Caplan; Dr. Albrecht; Mr. Allen; Drs. AuBuchon, Gilcher, Gomperts, Guerra, Haas, and Hoots; Ms. Jones; Dr. Kuhn; Ms. O'Connor; Drs. Piliavin; and Mr. Walsh. Ex officio members present were Dr. Chamberland; COL Fitzpatrick; and Drs. McCurdy and Snyder. Also present were Dr. Davey, Dr. Nightingale, CAPT McMurtry, and approximately 50 members of the public. Drs. Busch, Epstein, Goosby, Penner, Secundy, and Schiff were unable to attend. Dr. Jesse Goodman represented FDA at the meeting.

The meeting began at 9:08 AM with roll call, announcements regarding conflict of interest, and welcoming from Dr. Caplan. Next, Dr. David Satcher, Assistant Secretary for Health and Surgeon General, addressed the Committee. Dr. Satcher reviewed the scientific evidence on which the recent FDA Guidance to Industry on variant Creutzfeldt-Jakob disease (vCJD) was based, and the scientific questions that remain about how vCJD might be transmitted. Dr. Satcher outlined steps the Department of Health and Human Services (DHHS) was taking to insure the adequacy as well as the safety of the blood supply. Dr. Satcher expressed concern about the current availability of plasma derivatives, and he expressed support for the Department's hepatitis C lookback initiatives. He concluded by emphasizing the persistent vigilance that will be necessary to maintain the safety of the blood supply in the future. Dr. Satcher then invited questions from the Committee. The text of his speech is appended at TAB A.

Dr. AuBuchon asked Dr. Satcher why the decision ob British donor deferrals had been made without input from the Committee. Dr. Satcher responded that the Committee had previously spoken on general issues of safety and specific issues of availability that related to this issue, and he felt that the Department's decision was in the spirit of these recommendations. Mr. Allen asked Dr. Satcher about the availability of funding for the general notification component of the hepatitis C lookback. Dr. Satcher responded that funds for all purposes were limited, but that the Department feels it will be able to carry out the program it has proposed. Dr. Gilcher expressed

his hope that British donors now deferred might be acceptable in the future, and Dr. Satcher reiterated his commitment to revisit this issue regularly and whenever new information became available. Dr. Caplan commented on the importance, in the face of potential shortages, of having good measures of blood availability. Dr. Satcher responded that the National Heart, Lung, and Blood Institute (NHLBI) of the NIH had committed funds to address this issue. Dr. Guerra asked Dr. Satcher to comment on how best to communicate risks, particularly potential ones, to the public and at the same time maintain public trust in important public health programs. In response, Dr. Satcher discussed how the Department was handling the issue of vaccines that contain thiomersal as a preservative.

Dr. Nightingale read the Secretary's letter of July 15, 1999 to Dr. Caplan into the record. The Secretary directed the Committee to monitor closely current trends in blood donation and demand. She concurred with the Committee's recommendation regarding blood donation by individuals with hemochromatosis. The text of her letter is appended at TAB B.

I DEFERRAL OF BLOOD DONORS WHO HAVE RESIDED OR TRAVELED IN THE UNITED KINGDOM FOR A CUMULATIVE SIX MONTHS OR MORE BETWEEN JANUARY 1, 1980 AND DECEMBER 31, 1996.

Dr. Dorothy Scott of FDA reviewed the August 17, 1999 FDA Guidance to Industry on this issue. Dr. Scott noted that the Guidance also recommends deferral if an individual had used injectable products, such as bovine insulin, from Bovine Spongiform Encephalopathy (BSE)-endemic countries, and she discussed labeling of non-implicated blood products for the theoretical risk of CJD and viral transmission. Dr. Scott noted that comments on the Guidance would be discussed at the next Blood Products Advisory Committee (BPAC) meeting.

Dr. Davey expressed concern that diabetic donors would not know if some of their insulin had come from a BSE-endemic country. Dr. Gilcher commented that his blood center defers diabetics who are being treated with insulin. In response to a question from Dr. Hoots, COL Fitzpatrick noted that the Department of Defense continued to state its opposition to the deferral policy, but that it would comply with the guidelines as published when they become final. In response to a question from Ms. Jones, Dr. Scott noted that it was not the intent of FDA to require inclusion of every risk in a product label; instead, CJD was being included as an example of a risk. Dr. Caplan asked for clarification of how cases of vCJD, as opposed to classic CJD, would be identified; Dr. Chamberland briefly outined CDC surveillance programs for these diseases. Dr. Hoots emphasized the importance of communicating to the public that our understanding of the transmissible spongiform encephalopathies (TSEs) is a dynamic process, and that our understanding, and actions based on that understanding, will continue to evolve as new information becomes available.

Dr. Nightingale read a memorandum dated August 10, 1999 from Dr. Claude Lenfant, Director, NHLBI, to Dr. Ruth Kirschstein, Deputy Director, NIH, regarding the NHLBI intent to commit up to $300,000 annually to support monthly collection of data on the adequacy of the United States blood supply. Dr. McCurdy observed that the definition of "adequate" is blood group- and component-specific, and not as simple as it appears. He discussed various approaches to

monitoring the blood supply, and how to begin doing so as quickly as possible.

Dr. Gilcher commented that his blood center routinely collected much of the information that Dr. McCurdy had mentioned; Dr. Davey commented that the Red Cross would have similar data available. In a discussion of inventories, Dr. Gilcher noted that on the day of the Oklahoma City bombing, about 350 units of blood in excess of usual demand were used within four hours, and it had been essential that these units were actually in inventory. Ms. Marian Sullivan of the National Blood Data Resource Center then discussed her organization's data collection efforts, including those to be performed in collaboration with NHLBI.

CAPT Mary Gustafson of FDA discussed a letter dated August 10, 1999 from FDA Commissioner Jane Henney, M. D. to Dr. Satcher regarding FDA policy on blood donations from individuals with hemochromatosis. The letter states that for blood establishments that can verify that they provide therapeutic phlebotomy for hemochromatosis at no expense to the patient, FDA will consider case-by-case exemptions to existing regulations that require disease-state labeling and limit the frequency of blood collections. Any exemption will be accompanied by a request that safety data be collected. Upon a finding that undue financial incentives have been removed and that surveillance data is favorable, FDA can propose revisions to existing regulations. The letter notes that any proposed funding of therapeutic phlebotomy would have to be reviewed to determine its adequacy in removing financial incentives. The full text of this letter is appended at TAB C.

CAPT Gustafson clarified that the data collection would take place after the exemption was granted, because at the present time FDA does not feel there is an inherent risk in this population. In response to a question from Dr. Hoots, CAPT Gustafson noted that the FDA does not restrict the age of blood donors, although the standards of the American Association of Blood Banks (AABB), and age requirements for informed consent, have this effect.

CAPT Gustafson then reviewed the Public Health Service (PHS) Report commissioned by Dr. Satcher on strategies for increasing the blood supply. She noted the participation of the blood industry in the development of this report. The core recommendations of the report were to

1. Monitor the blood supply on an ongoing basis.
2. Encourage more donations by eligible donors.
3. Improve donor relations to facilitate recruitment and retention.
4. Remove restrictions to safe donations
5. Address economic issues facing the blood industry.

CAPT Gustafson noted that specific initiatives in each of these areas were already under way. The full text of this Report is appended to this summary at TAB D.

In the public comment period, Ms. Kay Gregory of AABB noted their opposition and that of America's Blood Centers (ABC) and the American Red Cross (ARC) to deferral of donors who may have been exposed to injectable drugs manufactured from cattle raised in BSE-implicated countries. At the same time, she expressed AABB support for the recommendations of the PHS

Report, many of which were also prior AABB recommendations. Ms. Gregory also stated that AABB supported the FDA approach to blood donations by individuals with hemochromatosis.

Ms. Kristin Smith of ABC requested that the Department of Health and Human Services develop a national campaign to increase blood donations. ABC requested a steady stream of messages from high-ranking government officials regarding blood donation, and government funding to support proven techniques for increasing blood donation. ABC then asked DHHS to remedy the time lag between the implementation of new blood safety measures and proportionate increase in third party payments for these measures. ABC also asked DHHS to develop a professional education program of blood use, and educational materials for deferred donors. Finally, ABC asked DHHS to publish the circumstances under which it would rescind its current guidance on British donor deferrals.

Dr. Paul Holland of the Sacramento Medical Foundation Blood Center expressed his strong opposition to the British donor deferral policy. Dr. Holland queried whether this policy was enforceable when stated only in Guidance form. CAPT Gustafson cautioned against a simplistic response to this question.

Dr. Paul Cummings described preliminary results of a proprietary computer-assisted donor screening program. Ms. Jan Hamilton of the Hemophilia Federation of America discussed efforts by her organization to promote blood donation. She stated that

> ... we asked for stricter guidelines, we got stricter guidelines, and we must stand behind them and do our part to see that the 2.2 per cent decline in donations is overcome.

Mr. Patrick Collins of the National Hemophilia Foundation also supported the British donor deferral policy.

After lunch, Dr. Caplan invited motions from the floor. Dr. Piliavin moved, and Ms. O'Connor seconded, a motion that *the Advisory Committee concurs with the guidelines that have been put forth regarding vCJD donor exclusion.* In the extensive discussion that followed, several members stated that they did not feel well enough informed on this issue at this time to vote on it. *Five of the fourteen present members of the Committee voted in favor of the motion, three against, and five abstained. The Chairman did not vote.*

Dr. Caplan then proposed, and Dr. Hoots seconded, a motion that *the Advisory Committee requests that it be advised at each meeting about the status of the British donor deferral policy and its impact. The motion was approved unanimously.*

II CURRENT AVAILABILITY OF BLOOD PRODUCTS

Mr. Dennis Jackman of the International Plasma Products Industry Association (IPPIA) noted that the industry had responded to previous recommendations by the Committee to publish monthly production figures, develop emergency supply programs, expand capacity, comply with good manufacturing practices, pursue research, and explore importation of products to alleviate

shortages. Mr. Jackman emphasized a point made earlier in the meeting by the blood industry that product availability was itself a safety issue. He noted that the plasma industry was in ongoing discussions with FDA about algorithms for managing post-donation information, and he was hopeful that the pace of regulatory review of therapeutic biologics could be accelerated.

In response to a question from Mr. Allen, Mr. Jackman noted that there were legal constraints on industry collaboration to project demand, and that measurement of future demand was inherently imprecise.

Mr. Larry Guiheen of Baxter then reported that his company had completed the three initiatives to increase production it had announced to the Advisory Committee in April 1998. These were licensure of an additional production facility, licensure of a new plasma purification process, and importation from his company's European facility. Mr. Guiheen estimated that these steps would increase Baxter's production by 30% in 1999 and by an additional 30% in 2000.

Dr. Jerry Winkelstein of Johns Hopkins University and the Immune Deficiency Foundation (IDF) reviewed the needs of individuals with the roughly 70 characterized immune deficiencies for plasma derivatives. He noted that these diseases are not rare - collectively, they are more common in children than leukemia and lymphoma; that - in part because of effective treatment - there are more adults than children with these diseases; and that - again because of effective treatment - individuals with these diseases can usually hope to live full, productive lives. As an example, Dr. Winkelstein noted that the first patient with Bruton's x-linked agammaglobulinemia had become a successful investment banker. Dr. Winkelstein noted that the efficacy of intravenous immunoglobulin (IVIG) in various immune deficiency states had generally been shown by comparing health status and outcomes of affected individuals during the time product was available and during the time product was not available, or by correlating health status and outcomes to trough levels of immunoglobulins in serum.

Dr. Winkelstein noted that the health status of most individuals with immune deficiencies permitted them to infuse themselves at home. He then presented the results of consecutive surveys by the IDF that indicated that the availability of IVIG had improved but was not yet adequate. Dr. Winkelstein cited various maneuvers that patients and providers were taking to deal with residual shortages, such as reducing the dose of IVIG or prolonging the interval between doses. One third of the physicians surveyed felt that the health of their patients was suffering because of the persistent shortfall.

In response to a question from Mr. Walsh, Dr. Winkelstein stated that the IDF does have a physician, though not a patient, registry for immunodeficiencies, and that the IDF plans to expand this activity, partly in collaboration with the ARC, to monitor the long-term effects of IVIG therapy.

Mr. Thomas Moran of the IDF then emphasized the concerns of the patient community over the facts that, while IVIG production appeared stable in 1999 at roughly 15,700 kg/year, this remained substantially below 1997 production of roughly 17,000 kg/year. He expressed relief that Baxter production was projected to increase, but concern over closure of other

manufacturing facilities. He requested that the government fund a study to determine the health consequences of the current IVIG shortage, and to make this a component of a surveillance program to monitor the health status of the immune deficient population. He also requested continued industry support for emergency allocation programs, and to address the needs patients who move - or who are forced by unavailability of IVIG to move - from one part of the country to another. He also requested further acceleration of the review of IVIG experimental protocols, licensure applications, and product releases by FDA.

Ms. Nancy Beulow of the Alpha One Association then presented a patient perspective on the shortage of alpha-1 antitrypsin. She began by noting that a full prescription dose of alpha-1 antitrypsin had not been available to any patient for two years, and than many patients could obtain no product whatever. She expressed particular concern about the rate at which new products to treat alpha-1 antitrypsin deficiency were being developed. She also expressed concern that proposed ambulatory procedure classification (APC) reimbursements would further limit patient access to therapy.

Dr. Mark Brantly of the University of Florida reiterated Ms. Beulow's concern about the pace of development of new therapies. He encouraged industry to develop and share alternative sources for the intermediate plasma product used to make alpha-1 antitrypsin, and he encouraged the FDA to support the development of multiple formulations and delivery mechanisms of aerosolized alpha-1 antitrypsin.

Mr. Jackman returned to the podium to discuss reimbursement issues. He began by pointing out that even if production problems were solved, product would still be unavailable if providers, such as hospitals, did not have sufficient financial resources to stock these products. He then pointed out the negative impact of this situation, or the fear that this situation would develop, on capital investment in new production facilities. He pointed out that the HCFA proposed fee schedule would reduce the current HCFA fee schedule for the clotting factor needed by a hemophiliac with a clinically significant bleed from about $3500 to $99, and that comparable reductions were proposed for treatments of patients with immune and alpha-1 antitrypsin deficiencies. Mr. Jackman pointed out the differences between treatment with these agents and other infusion therapies covered under the same APC.

Mr. Jackman stated that Congress had mandated a pass through to hospitals for clotting factors used to treat hemophiliacs because it had found that hospitals were not stocking this product because of inpatient reimbursement policies. He suggested that proposed outpatient reimbursement policies would have the same effect, and he requested comparable relief for outpatient providers. He concluded by stating that the Secretary has the authority under the enabling legislation to exempt therapies as she sees fit, and he requested that she use this authority in this circumstance.

Ms. Anita Ducca of ARC provided comparable cost estimates, and she supported Mr. Jackman's positions and proposals. She also questioned whether HCFA cost estimation methodologies had systematically excluded bills submitted by the most severely ill patients from analysis.

Dr. Hoots noted the implicit assumption of HCFA methodologies was that all hospitals care for a comparable patient mix. He observed that this was not the case. He predicted that tertiary care hospitals already burdened with a disproportionate load of patients in need of plasma derivatives would have an even greater incentive under the HCFA proposals to discontinue providing services to these patients, and that comparable care would not become available elsewhere.

Dr. Robert Weinstein of St. Elizabeth's Hospital in Boston then spoke to the Committee. His first point was that carve-outs for a limited number of products would not address the needs of the many who needed comparable but different products or services, such as apheresis. He reiterated Ms. Ducca's concerns about the data on which HCFA cost projections were based. He stated an additional concern that these reimbursement policies would stifle innovation.

Dr. Weinstein predicted that hospitals might in response advise patients that they could not provide these treatments on an outpatient basis, but could on an inpatient basis. However, there would be no guarantee that reimbursement for inpatient treatment rendered would be provided, and the patient would have no insurance to cover the substantial costs of these therapies. Dr. Weinstein admitted that he did not know the answer to the problem that he had described, but he asserted forcefully that it was not the one proposed by HCFA. The meeting then adjourned until the following morning.

The first speaker on August 27 was Mr. Patrick Collins of the National Hemophilia Foundation (NHF). He noted that NHF supported previous comments on supply and on reimbursement by IPPIA, ARC, and Dr. Weinstein, and he expressed his satisfaction at the current level of interaction between patients and industry.

Mr. Walsh introduced the following motion:

> *Whereas the Advisory Committee on Blood Safety and Availability is dedicated to ensuring patient access to safe and effective plasma-based therapies, their recombinant analogs, and blood therapeutic alternatives; and*
>
> *Whereas the Committee recognizes that the proposed prospective payment system for hospital outpatient department services ("OPD services") under the Medicare program may unduly restrict access to those therapies; and*
>
> *Whereas the Committee concludes that exclusion of these therapies from proposed prospective payment system will protect patient access;*
>
> *The Advisory Committee on Blood Safety and Availability hereby recommends that the Secretary of Health and Human Services exercise her existing statutory authority to exclude plasma-based therapies, their biotechnology analogs, and blood therapeutic alternatives from the definition of "covered OPD services" under the Medicare hospital outpatient department prospective payment system. The Committee further recommends that the Medicare program separately reimburse for these therapies, when furnished in a hospital outpatient department, including emergency room, on a reasonable basis.*

Dr. Hoots seconded the motion. Dr. AuBuchon proposed that the motion be amended to add "human-derived biologicals" in front of the words "and blood therapeutic alternatives." There was discussion about whether to include blood products and plasma derivatives in one resolution or to make separate resolutions on each subject. Dr. Haas proposed, and Dr. Aubuchon seconded, a *motion to table the resolution under discussion until the hepatitis C lookback agenda item could be heard, and until the Committee had heard presentations from the floor on the proposed APC for blood products. The motion to table was unanimously approved.*

III STATUS OF HEPATITIS C LOOKBACK

Dr. Paul Mied of FDA then reviewed the June 1999 Guidance to Industry on this subject. He noted that the revised Guidance incorporates the recommendation of the Advisory Committee regarding repeatedly reactive EIA 1.0 screening tests with a signal to cutoff ration greater than or equal to 2.5. The Guidance now also recommends lookback for an indefinite period, as long as "electronically or other readily retrievable records" exist, because the previous cutoff for lookback would have provided limited scope for EIA 1.0-triggered lookbacks. The Guidance also specifies conditions for use of the recently licensed RIBA 3.0 test, and it provides additional time for the blood establishments to complete record searches for events prior to January 1988. The target for completion of patient notification by consignees is September 30, 2001. These modifications have been incorporated into a Proposed Rule that would codify the Guidance to Industry. This proposed rule was submitted to the Department in July 1999.

Ms. Gregory reported on behalf of an AABB, ABC, and ARC Interorganizational Committee on HCV Lookback on an AABB survey of the status of direct notification. Ms. Gregory first noted that this Committee had developed standard notification letters for both physicians and recipients, with the assistance of CDC. The Committee has also developed a flowsheet and an information packet for providers, and a list of resources for both providers and patients. Returning to the survey, Ms. Gregory noted an approximately 40% return rate. She then noted that, in April 1999, 27% of blood establishments reported they had completed their lookback; in July, that figure had risen to 43%. Also in April 1999, transfusion services reported that they had notified about 3,000 recipients; in July, that figure had risen to about 4,000.

Dr. Mary Chamberland reported on the status of the CDC general notification effort. She mentioned software CDC had developed to assist transfusion services monitor the status of their notification efforts, and to facilitate evaluation by CDC, FDA, and the Agency for Health Care Planning and Research of the direct notification component of the lookback effort. CDC hopes that preliminary data from this initiative will be available in January 2000. Dr. Chamberland then reminded the Committee of provider education programs that CDC had sponsored in the past two years in advance of the public education program. She then reviewed the rollout of the public education campaign on hepatitis C that was held at the National Press Club on May 5, 1999. This event, which was sponsored by CDC, was attended by the Surgeon General, Dr. Caplan, and many other stakeholders.

Dr. Chamberland presented examples of a print campaign to reach transfusion recipients who may be unaware of their risk; this campaign is to begin in September 1999. She also mentioned

CDC hotlines and web sites, and the desire of CDC to partner with non-governmental organizations to increase the impact of this campaign. Dr. Chamberland concluded by mentioning that CDC will fund three Epidemiology and Laboratory Capacity Sites demonstration projects to explore integration of hepatitis C initiatives with other infectious disease control activities, and that CDC is exploring the possibility of funding hepatitis C coordinators within state health departments.

Dr. Nightingale concluded the presentation of government activities related to hepatitis C by referring the Committee to a summary published in the June 30, 1999 Science of the Sixth International Conference on Hepatitis C, held at the NIH in June 1999, and a paper by Drs. Alter, Margolis, and colleages in the August 19, 1999 New England Journal of Medicine.

In the public comment period, Ms. Gregory stated the opposition of the Interorganizational Committee on HCV Lookback to the indefinite extension component of the June 1999 FDA Guidance to Industry. She also requested a rolling 10 year limit on any future lookbacks. Dr. Holland expressed doubts about the effectiveness of the lookback. Mr. David Cavanaugh expressed his concern about the timeliness of the implementation of the lookback, and concern whether there would be adequate funding for the public education effort that Drs. Alter and Margolis had designed. In response to a question, Dr. Mied clarified that the deadline for consignee notification had been extended by six months to permit completion of the extended search in all readily retrievable records, but all other timelines specified in the September 1998 Guidance were unchanged.

Dr. Caplan invited the Committee to make motions, and Dr. AuBuchon moved that *the Committee recommends that the Secretary direct FDA to construct the HCV lookback in accordance with the prior recommendations of the Committee. Dr. Piliavin seconded the motion. Ten members voted for the resolution, one against, and one abstained. One member had left the meeting prior to the vote, and the Chairman did not vote.*

The Committee then turned to testimony on the proposed APC 369, which covers blood services. Ms. Theresa Lauerhass of AABB expressed her opposition to the current formulation of this APC, which would bundle transfusion therapies with apheresis therapies. She disagreed with the data on which the reimbursement was based. She requested that the cost of the infused product, the infusion procedure, and overhead costs be reimbursed separately. She also objected to the reduction in reimbursement for multiple procedures, and she requested that reimbursement schedules be updated more frequently than every two years.

Ms. Anita Ducca of ARC expressed similar opinions. She emphasized the disparity of an order of magnitude between current charges for many blood related services and the proposed reimbursement under APC 369. Dr. Holland then expressed his concern that the proposed HCFA policy would make it impossible for hospitals to provide current services.

The Committee then *resumed discussion of the motion by Mr. Walsh* that had been previously tabled. Dr. AuBuchon proposed an amendment to Mr. Walsh's motion that, in addition to adding "human-derived biologicals" as previously proposed, would add the following paragraph to be

the third paragraph of the motion:

> *Whereas, the proposed reimbursement payment for therapies under APC 369, which involve the administration of human-derived biologicals, including blood. components, is inadequate and miscategorized, and therefore threatens patient access to quality and potentially life-saving blood-related therapies,*

Dr. Guerra seconded this amendment. *The amendment was approved unanimously.*

Dr. AuBuchon then moved, and Mr. Walsh seconded, an amendment to *remove the words "human-derived biologicals" from the motion and instead add the following paragraph to be the final paragraph of the motion:*

> *The Committee recommends that the Secretary use her existing authority to exclude therapies under APC 369 from the prospective payment system for hospital outpatient services and reimburse them on a reasonable cost basis.*

This amendment was approved unanimously.

Mr. Walsh's motion as amended was then approved unanimously.

Before consideration of the final agenda item, Dr. Nightingale thanked the seven Committee members whose terms will expire on September 30, 1999 for their service.

IV HOW SHOULD FEDERALLY MANDATED BLOOD SAFETY MEASURES BE FINANCED?

Ms. Nancy Edwards of HCFA began this session by providing a Medicare perspective on this issue. Ms. Edwards noted that HCFA implements Medicare, but that almost all of the implementation, as well as the exceptions, are dictated by statute. For example, the reimbursement of blood clotting factors outside DRGs is based on a 1989 law, and APCs are mandated by the Balanced Budget Act of 1997. This law specifies that HCFA was to use actual claims data from 1996 for Medicare beneficiaries to determine reimbursement. The original target for implementing a prospective outpatient payment system was January 1, 1999, but the expected implementation date is now estimated to be April 1, 2000.

Ms. Edwards noted that, during the last year, HCFA has met with virtually every industry group affected by the prospective outpatient payment system. Ms. Edwards indicated that these meetings will result in substantial changes to the final payment system, and she indicated that HCFA would ameliorate as best they could the concerns raised about blood-related APCs. However, Ms. Edwards also indicated that HCFA was not favorably inclined towards a pass-through for blood products.

Ms. Edwards indicated that many of the concerns about introduction of APCs had been expressed when DRGs were introduced, and those concerns proved unjustified. Dr. Hoots responded that

there may have been more excess money in the health care system then than now, and he asked what plans HCFA had to prevent hospitals from discontinuing care for rare, expensive diseases. Ms. Edwards responded by citing the extra money paid to teaching hospitals, and Dr. Hoots noted that a recent study had found substantial geographic disparities in these payments. In response to a question from Dr. Caplan, Ms. Edwards said there may need to be many more specific APCs for blood, and that HCFA was totally open to dealing with that possibility.

After lunch, Dr. Lou Rossiter of Virginia Blood Services proposed that HCFA should anticipate, and prospectively compensate for, the costs of any new blood safety measures expected to be enacted in the coming year. He justified this unique approach on the basis of the voluntary, "non-market" act of donation.

Dr. Nightingale asked Dr. Rossiter how he would ensure that the increased payment for services to the hospital industry would be passed on to the blood industry; Dr. Rossiter acknowledged that there was no assurance. Dr. Nightingale then asked Dr. Rossiter what might differentiate blood from other public goods or common resources that are shared, or from other voluntary donations, and Dr. Rossiter responded that blood was from one's own body. Dr. Guerra suggested that if access to freely donated blood were viewed as a right, there would be a societal obligation to provide access to it. Dr. Caplan then pointed out that if there were a right to access, there would be a responsibility to donate, and that would obviate the voluntary nature of the donation.

Dr. Paul Ness of Johns Hopkins University and AABB then stated the concern of the industry that inadequate reimbursement is likely to hinder patient access to quality care. He described the growing list of transfusion-based therapies and of safety measures that would not be covered by the proposed reimbursement schedules. He pointed out that there is currently no adequate system in place to insure that Medicare inpatient payments fairly reflect the value and costs of new blood products and services in a timely manner. He stated that the time lag between the introduction of a new therapy and revision of DRGs to recognize that therapy constrained innovation. He stressed that non-profit providers of blood services had limited reserves to cover the cost of therapeutic innovation. Dr. Ness proposed that the government recognize the "unique priority" of blood safety and availability by providing adequate reimbursement to permit providers to continue to take all appropriate steps to safeguard the blood supply and to develop the new technologies and services that enhance these efforts. If necessary to accomplish that goal, blood and related services should be reimbursed separately from DRG and APC categories. Furthermore, reimbursement for blood services should not be at the expense of other vital services.

Dr. Nightingale asked why, if health industries such as the pharmaceutical industry were able to set an introductory price for a new product and to raise it without government intervention, that the blood industry would not be able to do the same. Dr. Ness responded that increases in the price of blood were the result of government mandates. Dr. Nightingale pointed out that other industries were subject to government mandates; Dr. Ness responded that other industries were not subject to a "zero risk" mandate. Dr. Nightingale pointed out that the airline industry, for one, was so situated. Dr. Hoots pointed out that in the case of blood, the government was both mandating increased costs for a service and, at the same time, decreasing reimbursement, and

that the Committee needed to get out the message that this situation was untenable.

Dr. Caplan proposed a motion that *the Committee recommends that the Secretary work with Congress to seek additional resources to support the introduction and maintenance of mandated blood safety measures. Dr. Hoots seconded the motion. The motion passed unanimously.*

Mr. Walsh proposed a set of motions related to the IVIG and alpha-1 antitrypsin shortages. There was extensive discussion of the specific wording of these motions. Dr. Nightingale summarized the sense of these motions as saying that in April 1998 the Advisory Committee made a set of recommendations about the availability of plasma derivatives. These recommendations have been mostly adopted, and the situation has improved, but it is still not satisfactory. The basic cause of the shortages is limited domestic manufacturing capacity; imports do not presently appear capable of fully compensating for domestic shortfalls. A related concern is the effect of current and proposed reimbursement practices on capital investment in new manufacturing facilities. Dr. Nightingale noted that it is standard practice to permit statements by members to be introduced into the record for up to 28 days after a meeting. Mr. Walsh then withdrew his motion.

Mr. Walsh then moved that *the Committee remains concerned about the continued shortage of intravenous immunoglobulin and alpha-1 antitrypsin despite laudable efforts on the part of both industry and government, and the Committee would support new as well as continuing efforts to alleviate these shortages. Dr. Piliavin seconded the motion. It passed unanimously.* The meeting was then adjourned at 3:23 PM.

This summary was approved by the Chairman of the Committee on September 2, 1999. It incorporates:

TAB A:	Text of remarks to the Committee by the Assistant Secretary for Health and Surgeon General
TAB B:	Text of letter dated July 15, 1999 from the Secretary to the Chairman of the Advisory Committee
TAB C:	Text of letter dated August 10, 1999 from the Commissioner of the Food and Drug Administration to the Assistant Secretary for Heath and Surgeon General
TAB D:	The Report of the Public Health Service Working Group on Strategies for Increasing the Blood Supply

The transcript of this meeting is available on the Committee's web site: www.dhhs.gov/partner/bloodsafety

TAB A:

Text of remarks to the Committee by the Assistant Secretary for Health and Surgeon General

REMARKS OF

DAVID SATCHER, M. D., Ph. D.

ASSISTANT SECRETARY FOR HEALTH AND SURGEON GENERAL

TO THE

ADVISORY COMMITTEE ON BLOOD SAFETY AND AVAILABILITY

THURSDAY, AUGUST 26, 1999

Good Morning. We have a lot to talk about today.

The first item on our agenda is the Guidance to Industry that the FDA issued on August 17. That Guidance relates to deferral of blood donors who have resided or traveled in the United Kingdom for a cumulative six months or more between January 1980 and December 1996. Let me address some of the concerns that this action has raised.

We are deferring blood donors who lived in the United Kingdom around the time of the "mad cow" epidemic. Mad cow disease first appeared there in 1985, a few years after a change had occurred in how cattle feed was prepared. In 1988, the use of certain animal products in cattle feed was banned, and the mad cow epidemic subsequently receded. It now seems clear that mad cow disease was transmitted by contaminated feed; but there may have been other ways it was transmitted as well.

New variant CJD appeared in the United Kingdom in 1995, ten years after the appearance of mad cow disease. New variant CJD is the human counterpart of mad cow disease. Forty-one of the 43 victims of new variant CJD, the total so far, have lived in the United Kingdom for at least ten years between 1980 and 1996; one other lived in France, and the last, an Irish citizen, appears to have spent substantial time in the United Kingdom. It seems likely that the agent that causes mad cow disease crossed the species barrier from cattle to humans in food; but again, there may have been other ways it was transmitted as well.

The greatest uncertainty at present is the number of United Kingdom residents who will eventually develop new variant CJD. Cattle develop symptoms about five years after exposure. If the incubation period in humans is also five years, and no further transmission takes place, there could be less than 500 cases. However, if the incubation period is much longer, far more could be affected. A test to detect individuals at risk of developing new variant CJD might settle this issue, but that test is not yet available.

There are other uncertainties as well. The new variant prion, for example, has been detected in the tonsils and the appendix of individuals before any symptoms of new variant CJD had developed. Can presymptomatic individuals transmit this disease? In the case of classic CJD, we have extensive epidemiologic evidence spanning three decades that conclusively demonstrates that this does not occur. In the case of new variant CJD, however, we do not have a corresponding assurance.

At present, the only way to reduce the possibility that the agent that causes new variant CJD might be transmitted in blood transfusions is to defer any blood donor who might be capable of transmitting this agent.

This action was first proposed by the FDA Transmissible Spongiform Encephalopathy Advisory Committee, or TSEAC, on December 18, 1998. At that time, the TSEAC recommended that this action not be implemented until its impact had been assessed. We concurred with that decision. On June 2, 1999 the TSEAC reviewed detailed estimates from the blood industry on the impact this recommendation would have. Essentially, these estimates were that a one-year residence-based deferral would eliminate 1.5% of donations, and that a six-month residence-based deferral would eliminate 2.2% of donations. TSEAC then reaffirmed its prior recommendation to defer, and polled its members individually on the duration of residence that would trigger deferral.

Because of the obvious urgency of this issue, the Department moved rapidly to consider it. The Blood Safety Committee, which I chair, met on June 8 to consider the TSEAC recommendation, and they unanimously supported it. The Blood Safety Committee also voted unanimously in favor of the six-month residency trigger. I accepted the Blood Safety Committee's recommendation, and communicated my support of it to FDA. FDA in turn announced its plan to implement this recommendation on June 17, and their Guidance to Industry was issued on August 17.

We plan to monitor the impact of this policy very carefully, and you will hear a more detailed

description of our monitoring plans later this morning. We remain committed regular review of this policy, and to updating it as soon as new scientific information becomes available. We will also continue our support of research into the cause, transmission, and treatment of all the transmissible spongiform encephalopathies, including but not limited to new variant CJD. We will also continue our support of research into the most effective means of promoting blood donation. Furthermore, the senior management of the Department, myself included, are willing and in fact eager to participate in appropriate industry-sponsored programs to increase blood donations.

I appreciate the effort you made last April to examine the reserve capacity of the blood supply. We have acted on the recommendation that you made. I also appreciate the effort of the Public Health Service Working Group that I commissioned to investigate this matter, and we will act promptly on their recommendations as well. I look forward to receiving any additional suggestions that may arise from your deliberations this morning, or in the future.

This afternoon you will receive an update on the availability of plasma derivatives, and the steps that have been taken to improve this situation. I remain concerned about the quantity of these products that is available, and I would like you to consider carefully how this situation could be further improved.

You will also hear an update on the progress of the hepatitis C lookback. This update will include the revised Guidance to Industry that FDA published on June 17, and CDC plans for general notification, tracking the progress of direct notification, and evaluating the success of these efforts.

Tomorrow morning you will consider the issue of how federally mandated blood safety measures should be financed. I'm sure this discussion will be lively, and I expect it to be constructive.

As you engage in this discussion, however, I want you to remember the following point. The blood supply is as safe as it is because we have worked very hard to make it safe. We also need to remember that there is no guarantee that it will remain safe unless we maintain our vigilance.

I would be glad to answer any questions you may have.

TAB B:

Text of letter dated July 15, 1999 from the Secretary to the Chairman of the Advisory Committee

THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

JUL 15 1999

Dr. Arthur Caplan, Chairman
Advisory Committee on Blood Safety and Availability
Center for Bioethics
University of Pennsylvania School of Medicine
3401 Market St., Suite 320
Philadelphia, PA 19104

Dear Dr. Caplan,

Thank you for your thoughtful letter summarizing the deliberations of the Advisory Committee on Blood Safety and Availability on April 29 and 30, 1999. These deliberations concerned the reserve capacity of the United States blood supply, and what steps could be taken to strengthen it. In view of our recent decision to defer blood donations from individuals who have resided in the United Kingdom for more than six months, your discussions were particularly timely.

I appreciate your concerns regarding current trends in blood donation and demand. Your Committee should monitor this situation closely, just as you are monitoring the supply of plasma derivatives and the progress of the hepatitis C lookback effort. The additional resources needed to accomplish this task should be addressed with the operating divisions that sponsor your Committee.

I also appreciate Dr. Schreiber's analysis of how we might correct the decline in blood donations by focusing additional efforts on retention of first-time donors. At the same time, it would be premature to depend on a single strategy to increase donations, so I also concur with your recommendation regarding blood donations by individuals with hemochromatosis. I am directing the Health Care Financing Administration and the Food and Drug Administration to identify strategies that would implement this recommendation.

I am sensitive to the issues that you raise in your letter regarding the potential impact of the current economic transformation of medicine on the safety and availability of the blood supply. These issues are currently under review within the Health Care Financing Administration, and you should anticipate a presentation of the issues from Medicare's perspective at your next Advisory Committee meeting.

Sincerely,

Donna E. Shalala

TAB C:

Text of letter dated August 10, 1999 from the Commissioner of the Food and Drug Administration to the Assistant Secretary for Heath and Surgeon General

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

TO: Assistant Secretary for Health and Surgeon General

FROM: Commissioner of Food and Drugs

SUBJECT: Blood Donations by Individuals with Hemochromatosis

This memorandum is in response to your memorandum dated July 21, 1999. You asked FDA and HCFA to identify strategies that would implement the recommendations of the Advisory Committee on Blood Safety and Availability (ACBSA) regarding blood donations by individuals with hemochromatosis.

On April 29, 1999, the ACBSA recommended that the Department of Health and Human Services "create policies that eliminate incentives to seek donation for purposes of phlebotomy" from patients with diagnosed hemochromatosis who require obligate phlebotomy as therapy for their disease. Further, as undue incentives to donate blood for transfusion (rather than being therapeutically phlebotomized) are removed, the Department "should create policies that eliminate barriers to using this resource." On July 15, 1999, Dr. Shalala wrote to Dr. Arthur Caplan, Chairman, ACBSA, informing him that she concurred with the Committee's recommendation regarding blood donations by individuals with hemochromatosis. She also advised that she was directing HCFA and FDA to identify strategies that would implement this recommendation.

Based on a consideration of this issue within FDA's Office of Blood Research and Review, FDA's Center for Biologics Evaluation and Research (CBER) is committed to the following course of action:

1. For blood establishments that can verify that therapeutic phlebotomy for hemochromatosis is performed at no expense to the patient, FDA will consider case-by-case exemptions to existing regulations. Current regulations require disease-state labeling for units from such collections to be released for transfusion [21 CFR Part 640.3 (d)] and limit the frequency of whole blood collections [21 CFR 640.3(f)]. FDA has the authority to permit exemptions to the blood regulations under the provisions of 21 CFR 640.120.

2. As part of any exemption to blood labeling and/or frequency of collection approved under 21 CFR 640.120, FDA will request that safety data be collected and submitted to the Agency. The data to be submitted will include viral marker rates, incidence of transmissible infections based on rates of seroconversion to viral markers, frequency of post-donation reports of undisclosed risks, and reports of donor and recipient adverse events. These data will be compared with comparable data obtained on the general donor pool.

3. FDA will review any funding plan proposed by HCFA to determine its adequacy in removing the financial incentive for persons with hemochromatosis to donate blood for transfusion. At the April 29 meeting, Dr. Al Grindon, from the Atlanta Region of the American Red Cross, reported that the patient charge for therapeutic phlebotomy ranges from $52.00 to $90.00. If less than full reimbursement is established for this procedure, the fact of a remaining charge and inconvenience to patients could leave open the question of an undue donor incentive. The possibility that some patients could remain without coverage by either medicare or private insurance would also need to be considered.

4. Upon a finding that undue financial incentives have been removed for therapeutic phlebotomies of hemochromatosis patients, and with favorable outcomes of surveillance data obtained under 21 CFR 640.120 exemptions to 21 CFR 640.3 (d) and (f), the Agency can propose revisions to the regulations. Such revisions would allow therapeutically obtained blood from hemochromatosis patients to be used without disease-state labeling and allow hemochromatosis patients to be phlebotomized for collection of transfusion products more frequently than once every eight weeks without examination by a physician at each phlebotomy event.

Please let me know if you need any further information on this issue.

Linda A. Suydam for
Jane E. Henney, M.D.

TAB D:

The Report of the Public Health Service Working Group on Strategies for Increasing the Blood Supply

STRATEGIES FOR INCREASING THE U. S. BLOOD SUPPLY

SUMMARY

At the request of the Assistant Secretary for Health and Surgeon General, David Satcher, M.D., Ph.D., who serves as the Blood Safety Director, the Interagency Working Group on Blood Safety and Availability convened an *ad hoc* task group representing Public Health Service (PHS) agencies, Department of Defense, and selected members of the Food and Drug Administration's (FDA) Blood Products Advisory Committee (BPAC) to advise the PHS Blood Safety Committee on national strategies that may be undertaken to increase the blood supply. The group met by teleconference five times (June 24, 28 and 29 and August 4 and 9, 1999). The group recognized the expertise, experience and insight of the blood industry in identifying problems in the supply and demand for blood. Therefore, representatives of the blood industry were invited on a one-time basis to provide input and comment.

A variety of problems contributing to blood shortages were identified. The problems include the low numbers of people who donate blood on a routine basis, the lack of a national monitoring system for blood collection and usage, and restrictions on donations from some potential donors that may not be necessary to protect the public health. The group recognized that not all problems can be readily solved but have identified some strategies for approaching solutions that can be achieved on a short-term basis. The Department of Health and Human Services (DHHS) should demonstrate leadership in fostering cooperative efforts to maintain adequate supplies of blood across the nation.

Strategies to increase the blood supply will require cooperation between the government and the industry. Possible short-term strategies may include participating in a possible industry sponsored media outreach campaign to encourage blood donations; co-sponsoring a public workshop to help better define the problems and share ideas for solutions; and providing public support for the current monitoring effort of the National Blood Donor Resource Center. Other strategies will take a longer time to plan, develop, implement and evaluate. The longer term efforts may include additional donor outreach activities, including educational efforts and customer relations improvements; removal of restrictions on donation from donors who are considered safe but currently deferred from donation; additional blood usage monitoring; and development of therapeutic alternatives to blood.

BACKGROUND

Transfusion of allogeneic blood and blood products is one of the most important medical interventions used to treat patients facing acute, life-threatening situations such as trauma, major

surgery and chemotherapy or who require chronic blood component replacement. The United States program to provide patients with these critical transfusion products is based almost entirely on individual volunteerism. Potential blood donors most often are made aware of the need for blood donation through community outreach by local blood banks. In spite of the urgent need for this resource, safety considerations prevent some potential donors' blood from being used. To maintain the safety of this important resource and the health of blood donors, blood collection centers utilize criteria for the selection of donors and perform laboratory testing on donor blood samples (including various tests for infectious diseases). Recent estimates have suggested that the rate of blood donations may not be sufficient to keep pace with an increasing demand.[1] This disparity may be further intensified with additional deferrals that are to be recommended as a precaution against possible transmission of new variant Cruetzfeldt-Jakob Disease (nvCJD).

NvCJD was first recognized in 1996 in the United Kingdom (U.K.).[2] Laboratory and epidemiologic studies have linked nvCJD to an outbreak of bovine spongiform encephalopathy (BSE) in the U.K.[3,4] BSE infection in cattle appeared in the U.K. in 1980, peaked in 1992, and fell to low levels by 1996.[5] At meetings in December 18, 1998, and June 2, 1999, FDA's Transmissible Spongiform Encephalopathies Advisory Committee (TSEAC) recommended that, until more is known about the extent of the epidemic and transmissability of nvCJD by blood, donors should be deferred from donating blood if they have resided in the U.K. during the BSE outbreak.

At two recent public meetings [6/2/99 TSEAC and 4/29/99 PHS Advisory Committee on Blood Safety and Availability (ACBSA)], Ms. Marian Sullivan, Executive Director, National Blood Data Resource Center (NBDRC), reported information from a 1998 comprehensive survey of U. S. blood collection facilities and transfusion services. These data were compared with data collected in a 1994 survey of the blood supply. The NBDRC is an independent, not-for-profit corporation, conceived and funded by the American Association of Blood Banks (AABB). Some relevant information from the survey included:

1. There were 11.7 million allogeneic blood donations in 1997, a 0.3% decline from 1994.
2. Total whole blood collections (allogeneic, autologous and directed) showed a 5.3% decline over the same period because of large decreases in autologous and directed donations (autologous decreased by 36.5%; directed by 38.6%).
3. Blood utilization increased about 1% each year over this time period.
4. Preliminary linear extrapolation of the data suggested that demand will exceed supply sometime in the year 2000.

Additional presentations at the April 1999 ACBSA included data from the Retrovirus Epidemiology Donor Study (REDS). Dr. George Schreiber, Westat, Inc., who analyzed data collected as part of REDS, noted that although almost half of the U.S. population has donated blood,

only about 5% donate in any given year, the majority of them only once. Dr. Alan Williams, American Red Cross (ARC), discussed the industry's use of incentives and their effect on blood donation noting that incentives to donate are widely used and increasingly so used. Other representatives of the blood industry also commented on possible mechanisms to increase supply including: reducing the length of donor questionnaires, developing a defined, maybe even paid, donor pool, and reimbursing for blood transfusions at higher costs. The effects of cost and competition also were discussed during that session, and it was observed that the financial limitations of blood collection organizations tend to restrict donor recruitment efforts.[1]

On June 8, 1999, the Blood Safety Committee of the PHS endorsed the recommendations of the TSEAC regarding deferral of donors for exposure in the U.K. The Blood Safety Committee evaluated the available information and concluded that potential blood donors who had traveled to or resided in the U.K. for six months or more, cumulatively, from January 1, 1980 to December 31, 1996 should be indefinitely deferred. It has been estimated that this policy will decrease national blood donations by approximately 2.2% although the losses may be greater in some areas. The decision of the Blood Safety Committee was announced publicly at FDA's BPAC on June 17, 1999.[6] Recognizing that this decision will likely reduce the U. S. blood supply, the Assistant Secretary for Health and Surgeon General, Dr. David Satcher, directed the PHS Interagency Working Group on Blood Safety and Availability to develop a report on strategies to monitor and increase the U. S. blood supply.

An *ad hoc* subgroup comprised of representatives from FDA, the Centers for Disease and Prevention (CDC), the National Institutes of Health, National Heart, Lung and Blood Institute (NHLBI), the Department of Defense, and selected members of the BPAC was asked to develop these strategies. The group met by teleconference five times between June 24 and August 9, 1999, to propose and discuss various methods that might be applied to increase the national blood supply. In addition, representatives of the blood industry were invited on a one-time basis to discuss blood donor recruitment and retention issues. The industry representatives were from the ARC, America's Blood Centers (ABC), the NBDRC, and the AABB. (See Appendix A for task group members and industry participants.)

5. ISSUES and RECOMMENDATIONS

Any national program undertaken by the blood industry to increase the blood supply deserves the leadership and support of the DHHS. The task group recognized that the blood collection industry has excellent physicians, scientists, and other professionals, including skilled donor recruiters. It is

their knowledge and experience that will provide an important element of any national initiative to increase the blood supply. Successful implementation of any of the following approaches will require cooperation and coordination, both within the blood industry and with the PHS agencies.

It was the consensus of the task group that the use of unpaid donors is an important factor in the U. S. blood supply and has contributed fundamentally to the high level of safety that characterizes our blood products. Therefore, although the group acknowledged some successes in the use of paid donors for allogeneic transfusions, the proposed strategies presented are restricted to the recruitment of and collection from volunteer (unpaid) blood donors.[7] The group also concurred that all strategies should be initiated with a mechanism for prospective data collection so that effectiveness can be evaluated. The task group's specific recommendations are presented below (and presented in bulleted format in Appendix B):

1.

1. **Monitor the Blood Supply**

1.

Reliable, timely data on national and regional blood supply (collection) vis-à-vis blood use (transfusion) are unavailable. Although periodic retrospective surveys have documented collection and usage trends for specific time periods and seasonal variability is well known, there are no reliable national instruments for anticipating shortages with sufficient lead time to accomplish increased donor recruitment or deliberate redistribution of existing supplies.[1,9,10,11,12,13] In the past this effort has not been funded adequately by the private sector. It is essential that both industry and the PHS have timely access to the data to facilitate planning. With this goal, it is recommended that under interagency guidance an appropriate agency within PHS should arrange for ongoing, proactive monitoring of the nation's blood supply. The resulting information would be used by government and blood centers to forecast or rapidly identify shortages and implement timely remedies.

In the short-term, it seems most reasonable for the PHS to support the current, on-going monitoring efforts of the NBDRC. The task group was advised by Ms. Sullivan that it is the intent of the NBDRC to continue biennial surveys as long as the effort is funded. It was noted that the surveys conducted by NBDRC are designed for data collection compatibility with previously published surveys by Surgenor and others.[10,11,12,13] In addition to the biennial survey, NBDRC plans a "Quick Count" survey in September 1999 of 150 blood centers to assess availability of transfusion components. This will not include blood usage data from transfusion centers. Data should be analyzed by early November. Other NBDRC planned studies of donor

related issues, to commence in the fall of 1999, include an evaluation of the effects of donor incentives and intercenter competition on blood availability. Ms. Sullivan advised the group that it is feasible to set up an information system which would provide up-to-date blood supply information on a routine basis if NBDRC resources could be expanded or externally funded. The working group suggests that funding be provided initially to support monthly surveys of a representative sample of U. S. blood centers and transfusion services. Longer intervals (2-3 months) between surveys would not be sufficient to respond to shortages and may not reflect short term variability supply, e.g., seasonal variability or impact of new donor deferral recommendations.

The NBDRC appears to be the only readily available resource for national data collection at this time. The ARC may have internal data on blood collected in the ARC system, and the AABB operates a National Blood Exchange (NBE) with some data collection capabilities. However, resource sharing requests to the NBE represent a small, defined customer subset that likely would not be representative of the U.S.

It is important to note that currently the NBDRC survey results are available only to its members and only in summary form, with the exception that the NBDRC has made some trend data publicly available.[1,5] In order for the data to be useful to the DHHS, the data would need to be available to the DHHS and the public. Additionally, statistical analysis of the 1998 survey data is limited. Any proposal to fund the NBDRC should include the provision that the surveys be more frequent, subject to more extensive statistical analysis, and the results be made publicly available. While the group viewed support of the on-going effort as the most expeditious approach, it also concluded that the appropriate long-term strategy would be the use of competitive contracting under the direction of PHS to insure adequate monitoring of blood supply availability and use.

Encourage More Donations by Eligible Donors

It has been estimated that nearly half the population over age 17 has donated blood at least once. However, only 5% of that population donates blood in a given year. Among active donors the average number of donations per year has been consistent at 1.5 [1,8] These data indicate that the number of eligible donors in the United States is adequate to meet the country's blood needs. The problem of shortages can be solved by encouraging current donors to give blood more frequently and to recruit more eligible donors into the current donor pool. A 15% increase in the average number of donations per donor per year would increase the national supply by 10%.[1]

One way to do this would be to get many donors who donate only once or twice a year to give one more time. Beyond that, it is important to encourage a lifetime "habit" of donating by donors who have given once or twice.

One way to encourage donations is to publicize the need for donors. Any publicity campaign should focus on both the retention and increased participation of established repeat donors as well as the recruitment of lapsed and first time donors. An appropriate short-term strategy would be an industry developed, broad based, national media campaign to encourage volunteer blood donation. Where appropriate and strategic, the PHS can encourage such a campaign by the industry. For example, public service announcements by high ranking DHHS officials who would be readily recognized by the public could be provided.

An organized effort should be made to identify successful recruitment models. Various research activities can be supported by PHS agencies to determine why one or two time donors have not continued to donate and to see what measures (e.g., incentives, recognition, convenience) would encourage more frequent donations by current donors who give an average of only 1.5 times per year.

A long-term strategy would be to address the education of children to foster the civic responsibility to be blood donors. Public education starting in elementary school should be useful in developing positive attitudes toward donation.

Improve Donor Relations As Part of Recruitment and Retention

The blood supply is dependent upon the volunteerism of Americans; strategies that can be undertaken on a long-term basis should address customer service improvements.. There are competitive pressures to "volunteer" for many charitable causes; and Americans demand better customer service than in the past. Information from an earlier era indicates that few donors (only 2-3%) are lost because of a bad experience at the time of donation.[8,14] However, those studies are over twenty years old. Much has changed in donor interactions with increased donor deferral criteria and increased competition among blood centers for the same donors.[9] There is a need to determine if current donor practices are effective in encouraging and retaining blood donors recognizing the need to avoid undue incentives to donate.

The issue of donor relations is mostly in the purview of local blood centers, but there may be more similarities than differences from one region to another. The task group identified areas in which government can play a role. In the absence of current published studies, the PHS may co-

sponsor with industry, a public workshop for identifying "best practices" for donor recruitment and retention. In addition to sharing "best practices," the public workshop should address the need and study design of instruments to evaluate donor interactions since much available donor behavioral information is anecdotal.

Longer-term projects that can be undertaken nationally include simplifying the donor questionnaire and/or designing a simplified questionnaire for repeat donors. Davey, and others have reported that donors find the current questionnaire extensive, intrusive, and tedious for repeat donors.[1,9] The task group felt that the responsibility for this project should be shared within the PHS agencies.

Another longer-term project is the development of the computer-assisted donor history questionnaire. NHLBI is currently supporting a study that is presently in clinical trials phase (See appendix C for NHLBI studies). Once developed, the FDA can encourage its use by accepting the instrument and study data for use by blood centers.

2. Remove Restrictions to Safe Donation

1. Some healthy donors are restricted from donation for transfusion by existing government or blood center policies. The PHS should investigate whether all current deferrals are necessary to protect the public health. The country will soon enter a new era of improved infectious disease testing.. Currently, most blood centers are testing (under investigational protocols) and anticipate use of, nucleic acid testing (NAT) for HCV. Concurrently, many blood centers are also using (under investigational protocols) NAT for HIV. When new technologies such as NAT are licensed, a review of deferrals should be undertaken in the context of universal application of the technologies. Specific donor deferral issues which deserve review are discussed below:

Hemochromatosis

The PHS should move proactively to determine whether hemochromatosis patients can donate as normal donors. This patient group is very active and would like to be able to donate. Medical data support that hemochromatosis patients are not less safe donors because of their disease; however, there are questions about the voluntary nature of their donations because people with hemochromatosis require phlebotomy as therapy. The obligate need for phlebotomy introduces an incentive to donate blood for transfusion because most patients are charged for the therapeutic removal of blood. The concern is that a financial incentive to donate at no cost, rather than be phlebotomized therapeutically, might cause the donor to be less truthful about acknowledging risk behaviors. Removing patient cost for therapeutic

phlebotomy would alleviate that concern. To accomplish this, the DHHS must identify and remove barriers to providing reimbursement support for all therapeutic phlebotomies.

This action by DHHS can only be effective if changes in blood labeling are made in concert. If subjected to special labeling as presently required by blood regulations, the product probably will not be used. Currently, Title 21, Code of Federal Regulations, Part 640.3(d) requires the disease state to appear on the label of blood obtained therapeutically. FDA must determine if this regulation should be changed to facilitate use of blood from hemochromatosis patients, i.e., to allow blood from hemochromatosis patients undergoing therapeutic phlebotomy to be labeled no differently than blood from volunteer donors. Recent publications suggest that allowing hemochromatosis patients to donate may have a significant positive effect on supply.[15,16]

On the other hand, some estimates show that hemochromatosis patients already donate without revealing their diagnosis with the same frequency as hemochromatosis is detected in the population. If true, no effect the would be seen if hemochromatosis patients were officially entered into the donor pool.[17] Prospective studies should be undertaken to evaluate the frequency of donation and the viral marker rates from this population.

Donor re-entry – history of positive viral markers

Donor deferral policies are created with redundancies and the goal of preventing unsafe donors from re-entering the donor pool. Donors deferred in the past because of false-positive viral marker testing can be reinstated after additional testing following a defined testing protocol with interpretive algorithm. By their conservative nature, donor re-entry algorithms do not allow reinstatement of a proportion of past donors who are healthy but deferred because of viral marker testing results. FDA should review donor re-entry algorithms used to reinstate donors deferred because of testing to determine if changes can be made.

History of male / male sex

Donors are also deferred because of risk history. One risk deferral category is a male having sex with another male, even once, since 1977. If such risk is acknowledged, the donor is permanently deferred. At recent BPAC meetings and a public workshop, FDA has discussed whether the current deferral policy for males who have had sex with other males should be relaxed by some degree.[18] The BPAC made no decision on this issue but encouraged FDA to continue to gather information to address this question. FDA should continue to review this issue and modify the deferral policy, if warranted.

Hepatitis B core antibody

While the above donor issues can be addressed in the relatively near future, other deferral issues may be addressed in the long term. For example, donors who are hepatitis B core antibody (HBcAb) positive are currently deferred from donating transfusable blood components. However, it is possible that this policy would be changed based on adequate scientific data. It was suggested that the HBcAb testing offered only a limited benefit and about 0.5-1.5% of the donors exhibit reactivity. However, data are not available which specifically address the safety of eliminating this test. Also, there are no figures which indicate the number or percent of donors who are eliminated solely because of their HBcAb reactivity, especially after readjustment of the cut-off for the test to improve its specificity. The task group recommends further studies in this area.

Address Economic Issues Facing the Blood Industry

Throughout discussions, the task group and industry participants repeatedly expressed concerns about the economic distress of the blood industry. Reimbursement practices and competitive pressures of health care today make it difficult for blood banks to recover the cost of new innovations, even when such measures are required. These economic limitations are a strong disincentive for change. The task group recognizes that the economic issues associated with changes in the blood supply will be addressed at the August 26-27, 1999, meeting of the ACBSA.

2. CONCLUSION

As a result of its discussions, the task group recommends that the highest priority actions by the DHHS should be to monitor the blood supply and to encourage increased donations by eligible blood donors. Short-term strategies include government support of an on-going effort to monitor the blood supply; government cooperation with a yet-to-be-developed industry public relations campaign to encourage blood donations; and cosponsorship of a public workshop to identify "best practices" in donor recruitment and retention. Longer-term strategies include additional donor outreach efforts, including education and customer relations improvements; removing restrictions from donation for safe, but currently, deferred donors; and additional blood supply monitoring. The development of alternatives to blood therapies also may mitigate blood shortages but lies beyond the scope of this report.

The success of any national effort to affect the blood donor supply will depend on improving the bond between the blood industry and the blood donor community. Effective leadership by the government and cooperation of the blood industry are needed to ensure that the American public can depend on a safe and readily available source of blood therapies.

Appendices:

A—List of PHS working group members and industry resource participants

B—Bulleted report format

C—NHLBI Planned Studies

REFERENCES:

1. 4/29/99 ACBSA transcript
2. Lancet 1996 347:91-5
3. Nature 1996 383:685-690
4. Nature 1997 389:498-501
5. 6/2/99 TSEAC transcript
6. 6/17/99 BPAC transcript
7. Transfusion 1998 38:874-882
8. Technical Report 138 Operations Research Center MIT 1978
9. Blood Donors and the Supply of Blood and Blood Products IOM 1996
10. Transfusion 1998 38:625-636
11. New England Journal of Medicine 1990 322:1646-1652
12. Transfusion 1993 33:139-144
13. Transfusion 1995 35:802-812
14. Transfusion 1977 17:123-135
15. Transfusion 1999 39:651-656
16. Transfusion 1999 39:578-585
17. Transfusion 1999 39:551-553
18. 9/21/98 FDA Workshop Transcript

Appendix A:

Task Group Members

Mary Chamberland	Centers for Disease Control and Prevention
Kenneth Clark	Centers for Disease Control and Prevention
Teresa Finlayson	Centers for Disease Control and Prevention
Glen Fitzpatrick	Department of Defense
Lianne Groshel	Department of Defense
Stephen Nightingale	Department of Health and Human Services
Gilliam Conley	Food and Drug Administration
Jay Epstein	Food and Drug Administration
Mary Gustafson	Food and Drug Administration
Richard Lewis	Food and Drug Administration
Barbara Alving	National Heart, Lung and Blood Institute
Paul McCurdy	National Heart, Lung and Blood Institute
George Nemo	National Heart, Lung and Blood Institute

One Time Industry Participants

Kay Gregory	American Association of Blood Banks
Celso Bianco	America's Blood Centers
Susan Parkinson	America's Blood Centers
Richard Davey	American Red Cross
Brian McDonough	American Red Cross
Alan Williams	American Red Cross
Marian Sullivan	National Blood Data Resource Center

Appendix B

1. INCREASING THE BLOOD SUPPLY

At the request of the PHS Blood Safety Director, a task group representing PHS agencies, Department of Defense, and invited members of FDA's Blood Products Advisory Committee was convened to advise the Blood Safety Committee on strategies to increase the blood supply that may be undertaken, or augmented, as a national effort. The group views cooperation with the blood industry an important component of any national effort. Current problems identified by the group and recommendations follow.

A. **Problem:** Reliable, timely data on national and regional blood supply vis-à-vis blood use is unavailable. Although periodic retrospective surveys have documented collection and usage trends for specific time periods, and seasonal variability is well known, there are no reliable national instruments for anticipating shortages with sufficient lead time to accomplish increased donor recruitment or deliberate redistribution of existing supplies. In the past this effort has not been funded adequately from the private sector. It is essential that the industry and DHHS have timely access to the data to facilitate planning.

Solution: Provide ongoing, proactive monitoring of the nation's blood supply. The resulting information would be used by government and blood centers to forecast or rapidly identify shortages and implement timely remedies.

Strategies: Provide government support to monitor the blood supply.

Short-term – Fund ongoing National Blood Donor Resource Center survey efforts with statistical support and request for more frequent surveying.

Long-term – Sponsor a competitive contract for monitoring. Establish monitoring of the blood supply as a program under PHS oversight.

B. **Problem:** Although nearly half the people over age 17 have donated blood at least once, only 5% of that population donates blood in a given year. Among active donors the average number of donations per year has been consistent at 1.5.

Solution: Increase the number of donations per year by repeat donors. Encourage lifetime "habit" of donating by donors who have given once or twice. A 15% increase in the average number of donations per donor per year would increase the national supply by 10%. One way to do this would be to get many donors who donate only once (or twice) a year to give one more time.

Strategies: Publicize need for donors. Improve both the retention and increased participation of established repeat donors as well as recruitment of lapsed and first time donors.

Short-term – Encourage industry developed media outreach. Support outreach efforts by providing public statements by DHHS officials.

Long-term – Support research on one/two time donors to determine why they have not continued to donate; conduct research on current donors (who give 1.5x/year) to see what (e.g., incentives, recognition, convenience) would encourage more frequent donations. Support childhood education to develop lifelong donation practices; benchmark successful private efforts to determine if national program is possible.

C. **Problem:** The blood supply is dependent upon the volunteerism of Americans. People are busy; there are competitive pressures to "volunteer" for many charitable causes; Americans demand better customer service than in the past. Davey, and others have reported that donors find the current questionnaire extensive, intrusive, and tedious for repeat donors. However, the impact of current donor disenchantment, if present, is unknown

Solution: Improve donor relations and outreach..

Strategies: Much of the solution depends on local efforts. Some strategies mentioned above crosscut (i.e., incentives, recognition and donor convenience). However, there are identified areas in which government can play a role.

Short-term –Cosponsor public workshop for identifying "best practices" for donor recruitment and retention.

Long-term – Simplify the donor questionnaire and/or design a simplified questionnaire for repeat donors.

Support the development of computer-assisted donor history questionnaire and encourage its use.

Support research on effectiveness of customer service improvements.

D. **Problem:** Some healthy donors are restricted from donation for transfusion by government / blood center policies.

Solution: Ease restrictions on some donor deferrals. The impact of universal application of NAT testing should be considered as a basis to relax some deferrals.

Strategies: *Short-term* – Allow hemochromatosis patients to donate without prejudicial labeling of the blood component on a case-by-case basis if no financial incentive is present.

Long-term – Remove financial incentives for hemochromatosis donation by 3rd party/Medicare support of therapeutic phlebotomies.

Simplify donor re-entry algorithms.

Revise deferral for males who have had sex with another male to 5 years – or possibly shorter.

Encourage scientific studies to determine whether Anti-HBc positive donors may safely donate.

E. **Problem:** The economic and competitive pressures of health care today make it difficult for blood banks to recover the cost of new innovations, even when they are required.

Solution: Improve mechanisms by which the free market automatically can fund safety innovations.

Strategies: *Short-term* – Provide a public forum for discussion of economic challenges to the blood industry.

Long-term—Review government policies which affect reimbursement for blood products.

Appendix C – NHLBI planned studies

NHLBI Research Studies on Donor Recruitment, Motivation and Screening

With demand for blood increasing and supply decreasing, the AABB National Blood Data Resource Center estimates that overall demand will exceed supply in the year 2000. The recent decision of the U.S. Public Health Service to recommend deferral of donors who have visited and/or resided in the United Kingdom for a cumulative period of six months or greater between 1980 and 1996 will likely exacerbate this problem.

Understanding why people donate blood is paramount to insuring the adequacy and safety of the blood supply. The National Heart, Lung, and Blood Institute (NHLBI) through its Retrovirus Epidemiology Donor Study (REDS) plans to conduct a survey of donor motivations. Furthermore, the Institute plans to evaluate the use, effectiveness, and safety of blood donation incentives. A study is also being considered to determine the feasibility of increasing the frequency of donations in repeat blood donors by one donation per year. The Institute is also supporting a study that is evaluating a computer-assisted interactive video donor screening system. Brief descriptions of these studies follow.

1) Evaluation of the Impact of Recruitment Strategies on Blood Donation Behavior

Extensive literature exists on ways to recruit blood donors. However, few attempts have been made to study the real-time interactions of blood centers with their donors on a large scale, or to conduct controlled experiments to determine the positive and negative impact of specific recruitment programs, especially those offering various forms of incentives. The primary goal of this study is to produce measurable improvement in donor recruitment efficiency as measured by new and repeat donation behaviors in those subgroups, while monitoring any major changes in deferrable risk.
In Phase I of the study, REDS will interact closely with a small group of mobile blood collection units for approximately 6 months. The recruitment strategies used for donors at a sample of these mobile units such as tele-recruiting, direct mailing, and media appeals will be documented and donor responses to these recruitment strategies will be measured. A combination of mail and on-site survey techniques will be used to measure prevalence of deferrable risk and, donor attitudes and responses to recruitment practices.

Based upon data derived from previous REDS Donor Surveys and available data from Phase I, four REDS blood centers will implement and evaluate experimental incentive programs in Phase II of the study. In this phase, specific incentives and promotional strategies such as cholesterol testing, gifts, or time off from work will be provided to the same mobile units, with the goal of measuring the positive and negative impact of these specific interventions. Prevalence of deferrable risk and recruitment efficiency among sites that implemented new incentives programs will then be measured and compared to similar data obtained in Phase I before implementation of the incentives.

The survey instruments for this study are being developed. It is anticipated that the documents will be submitted to the Office of Management and Budget (OMB) in October 1999 and the study initiated in January 2000.

2) Study of Donor Motivations

Little appears to be known about what motivates some people to become regular blood donors, or why only about 39 percent of first-time donors return. Adequate information pertaining to donor motivation in various ethnic groups is also lacking; data which would be valuable for minority recruitment efforts. With the current difficulties in maintaining an adequate blood supply, it is important to discern the reasons behind people's decisions to donate, so that better recruitment strategies can be formulated.

The REDS group is in the process of developing a donor survey to examine motivational factors. The survey will be conducted at all five REDS blood centers at both fixed and mobile recruitment sites. Donors

will be presented with a questionnaire to be completed during the donation process. Previous REDS donor surveys have yielded low response rates from certain groups of donors, such as first timers, minorities, and the young. It is thought that using the approach of surveying donors while they are still at the center will increase response rates for these groups and be of minimal cost.

Approximately 37,000 donors will be surveyed over a 6-month period at the five REDS centers. The survey will be identity-linked to enable follow-up of donors in the REDS donation database. This will permit REDS investigators to compare actual donation behaviors to stated intent. Questions pertaining to motivational factors and demographic data will be collected. Blood centers will also track incentive use and recruitment techniques at both mobile and fixed sites to permit evaluation of the association between actual exposure to incentives and reported donor motivational factors.

The survey document is currently being developed and will be submitted the OMB in October 1999. The study is scheduled to begin January 2000.

3) Study to Increase Blood Donations

The Institute is currently considering initiating a study within its REDS program to increase the frequency of blood donations in repeat blood donors by one donation per year. For many years, data have repeatedly shown that most blood donors give but once a year (50-70%, most recent REDS data). If a second blood donation is given within 1-2 years of the first, the individual is more likely to become a "regular donor," defined as one who gives every 1-2 years for several years. It is hypothesized that arranging for donors who give 1-2 times yearly to donate blood once more per year is feasible and will increase the blood supply and eliminate shortages.

The study would be conducted in two or more REDS blood centers. For a sample of a blood center's fixed and mobile sites, arrangements would be made for each donor, while resting in the canteen after donating, to make an appointment for the next donation (after 3-6 months). A reminder (card and/or call) will be sent before the appointment. Control sites will have no such appointment plans. Endpoints would be the number of donations at the test sites with an appointment system, compared with those sites who use current procedures. A one year trial should be sufficient to determine the feasibility of this approach.

4) Computer-assisted Interactive Video Donor Screening

The Institute is supporting a grant program to develop an interactive, multimedia video blood and plasma donor health history system; and to evaluate its acceptance and feasibility in operational settings. The principal aims of the program are to improve overall operational systems for screening donors and collecting blood and plasma; and to improve the safety of blood and plasma supplies. These aims will be evaluated in two stages. In the initial stage, the interactive video screening software will have no decision logic and the nursing staff will determine donor suitability from the printed output of the screening system. In the final stage, it is planned to integrate the interactive video donor screening system into the data management system of the donor center resulting in a "paperless" health history assessment.